Original Research Article

CLINICAL, ENDOSCOPIC AND HISTOPATHOLOGICAL PATTERNS AMONG PATIENTS WITH DYSPEPSIA.

ABSTRACT

Aim: Dyspepsia is a term differently understood, and associated with various upper gastro-intestinal endoscopic and histopathologic patterns. Most patients have regarded upper abdominal pain as 'peptic ulcer disease' with resultant late presentation of upper gastro-intestinal malignancies in some cases. This study examined the clinical presentation, endoscopic and histopathological patterns among patients with dyspeptic symptoms in Nnewi, South-East Nigeria.

Methods: This hospital based descriptive cross-sectional study examined 352 patients presenting with dyspepsia. Abdominal ultrasound was used to exclude patients with dyspepsia of biliary or pancreatic origin. An interviewer administered questionnaire (using the short form Leeds dyspepsia questionnaire) was used to describe dyspepsia patterns, and gastroscopy done on the included patients following an overnight fast. Samples obtained from endoscopy were assessed histologically for morphology and presence of H.pylori organism.

Results: Most participants belonged to 55 to 74 years age group with a mean age of 52.27±2.59 years. Epigastric discomfort (96.9%), heart burn (63.1%) and belching (55.4%) were the commonest symptoms. The commonest endoscopy and histopathologic findings was chronic gastritis (63.06% and 51.99% respectively), although there was poor agreement between the two modalities.

Conclusion: Histology remains the goal standard for diagnosis. However,we recommend endoscopy for dyspeptic patients especially in the elderly to enhance early detection of cancers, which were significant in this study.

Key words: Chronic Gastritis, Clinical Presentation, Endoscopy, Histology, Pattern.

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INTRODUCTION

Robust and standardized clinical definition for dyspepsia remains elusive;[1] this term and the various qualifiers have been interpreted differently by both physicians and patients alike for years. Dyspepsia is a medical term for difficult digestion or indigestion. It includes various symptoms in the upper abdomen, such as fullness, discomfort, early satiation, bloating, heartburn, belching, nausea, vomiting, or pain.[1,2]

Dyspepsia is a common disorder with a prevalence of 12%, 8% and 8% in the adult population of USA, Canada and UK respectively.[3]In an endoscopic study done in northern Norway, 9% and 14% of those with epigastric pain had peptic ulcer disease (PUD) and oesophagitis respectively.[4]Several studies have shown that majority of dyspepsia are due to minor abnormalities of uncertain significance or an entirely normal endoscopy (labelled as functional or non-ulcer dyspepsia) while only a small fraction are associated with PUD, reflux oesophagitis and cancer.[5-6]

The experience in parts of Africa appears to be at variance with the above stated. Dyspepsia accounted for 10% of all hospital admissions in Kenya.[7]In a study carried out in an endoscopy unit among all patients requiring upper gastro-intestinal endoscopy in Sudan, 3% of the patients had normal findings, while gastritis, esophagitis, PUD, oesophageal varices and upper GI tumours (gastric or oesophageal) accounted for 54.9%, 42%, 21%, 13.8% and 13.3% respectively.[8]Madeha*et al*. in Egypt reported that 155 of the 188 (86.1%) patients presenting with dyspepsia had abnormal endoscopic findings and gastritis was the commonest histological finding in 68% of the patients.[9]

The prevalence of dyspepsia was reported to be between 35-48% in Nigeria.[10]It was found to be 64.6% among students in South Western Nigeria.[11]Higher frequency was seen among patients

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who were on aspirin which is a risk factor for dyspepsia.[12] A hospital based study done in the Lagos state university teaching hospital, South Western Nigerianby Hameed *et al*reported a prevalence of 29%,[13]while the reported prevalence in North Eastern Nigeria was 26%.[14]Prevalence of dyspepsia is reported to be significantly higher in women, smokers, non-steroidal anti-inflammatory drug (NSAID) users and *H. pylori*-positive individuals.[15]

There is paucity of documented information in Nigeria, especially South-East Nigeria about the symptom pattern, as well as endoscopic and histological patterns of dyspepsia. In our environment, a lot of patients presenting with dyspepsia are already convinced they have 'ulcer'. This trend has led to mismanagement and late presentation of certain diseases including gastric and other gastrointestinal cancers and liver diseases in some cases. This study is therefore aimed at determining the clinical presentation, the endoscopic and histologic patterns in patients with dyspepsia in Nnewi, South East Nigeria.

Methods

Study design/site: This was a hospital-based prospective descriptive cross-sectional study of 352 patients that presented to the gastroenterology and hepatology clinic of NAUTH and SalutemRapha Specialist Hospital (a private specialist gastroenterology and hepatology hospital) both in Nnewi Anambra State, Nigeria. Both facilities are equipped with endoscopic machinery and personnel. This was carried out over a period of twelve months.

Study population: All patients aged 15 years and above with symptoms of dyspepsia seen in the medical or surgical outpatient clinics or medical or surgical wards or referred from other centers for upper gastrointestinal endoscopy and who gave consent for the study were enrolled. The features considered as dyspepsia include heartburns, epigastric pain, etc. Patients aged below 15

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years, pregnant patients, dysphagia, prior diagnosis of PUD and cases of dyspepsia of pancreato-biliary origin were excluded from the study.

Sample size: The minimum sample size for this study was determined from the formula below[15]

$$n = \frac{Z^2pq}{d^2}$$

Where

n = minimum sample size

Z= constant at 95% confidence interval from Z table

p= prevalence of dyspepsia is 29%[12]

q= 1-p

d= precision at 95% confidence interval = 0.05

Calculation: $n = \frac{(1.96^2)\ (0.29)\ (0.71) = 0.79}{0.0025 \qquad 0.0025}$

=316

To compensate for non- response, the formula below was used, [15]

$$n_s = \frac{n}{a}$$

Where, n_s = sample size to be selected

n =original calculated sample size

a= anticipated response = 90%

Calculation: $n_s = \frac{316}{0.9}$

= 351.1

For the purpose of this study, 352 patients were recruited.

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Exclusion Criteria:

- Dysphagia
- Upper gastrointestinal bleeding
- Prior diagnosis of peptic ulcer either by endoscopy or barium studies
- Strong suspicion of cancer
- Incomplete procedure
- Relief with defecation or change in stool frequency or form
- Pregnancy
- Biliary and pancreatic disorders

Method: All patients had abdominal ultrasound to exclude dyspepsia of biliary or pancreatic origin. Patients recruited into the study were counselled on the procedures to be undertaken, gave consent (written consent) and had an overnight fast prior to gastroscopy. The hepatitis B, C and HIV status of the patients were also determined as part of pre-endoscopy screening test. An interviewer based short form Leeds questionnaire was used to obtain the socio-demographic data (age, sex, educational status, occupation, etc) and symptoms. Patients were given lidocaine spray to anesthetize the posterior pharynx. Following which the gastroscope was gently inserted up to the second part of the duodenum. The mucosa of the oesophagus, stomach, first and second parts of the duodenum were observed carefully: findings were documented, photographs taken and biopsy was taken from abnormally looking mucosa or obvious lesions. The gastroscope was then gently removed. An Olympus GIF-160 Video Gastroscope with 8.6mm Outer Diameter, 2.8mm Working Channel, 103cm Working Length, 140° Angle of View, Angulation 210°/90°Up/Down and 100°/100° Right/Left was used for this study. The obtained samples were placed in a

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specimen container with 10% neutral buffered formalin and sent to an experienced pathologist for histopathological evaluation and reporting..

Data analysis: Data entry and analysis was done using the statistical package for social sciences (SPSS) version 20 software (SPSS Inc, Chicago, IL, USA). Continuous variables expressed as mean ± standard deviation were compared using student t-test. Comparisons between different groupings of the sample for measurements were done using one way analysis of variance (ANOVA). Categorical variables were compared using chi-square (X^2) analysis for association using a 2 x 2 or 3 x 3 tables as considered appropriate. A p-value of less than 0.05 was considered statistically significant.

Ethical consideration: This was obtained from Nnamdi Azikiwe University Teaching Hospital Ethical committee (NAUTHEC) on 21st June, 2021 with ref no: NAUTH/CS/66/VOL.14/VER 3/173/2021/046. Informed written consents were obtained from the study participants.

RESULTS

There were three hundred and fifty-two (352) patients aged between 15 and 91 years in this study, most of whom were secondary school leavers (44.88%), traders (25.2%) and males (52.56%), with a male to female ratio of 1.1:1. The mean age of the patients was 52.27 ± 16.59 years. Most of the patients were aged between 55 and 74 years. (Table 1)

Table 1: Showing the socio-demographic distribution of study participants

Variable	Frequency	Percent (%)
Age (years)		
15-34	64	18.18

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35-54	128	36.36
55-74	133	37.78
75 years and above	27	7.67
Sex		
Male	185	52.56
Female	167	47.44
Educational level		
Primary	51	14.49
Secondary	158	44.88
Tertiary	139	39.48
None	4	1.14
Occupation		
Artisans	4	0.6
Business	179	25.2
Church worker	11	1.5
Dependent	47	6.6
Driver	2	0.3
Farming	7	1.0
Pensioner	4	0.6
Professionals	46	6.5
Retired	12	1.7
Self employed	2	0.3
Student	24	3.4
Unemployed	14	2.0
Total	**352**	**100**

We observed that incidence of dyspepsia increased with age, reaching a peak in the sixth decade of life and then, declined afterwards. (Figure 1)

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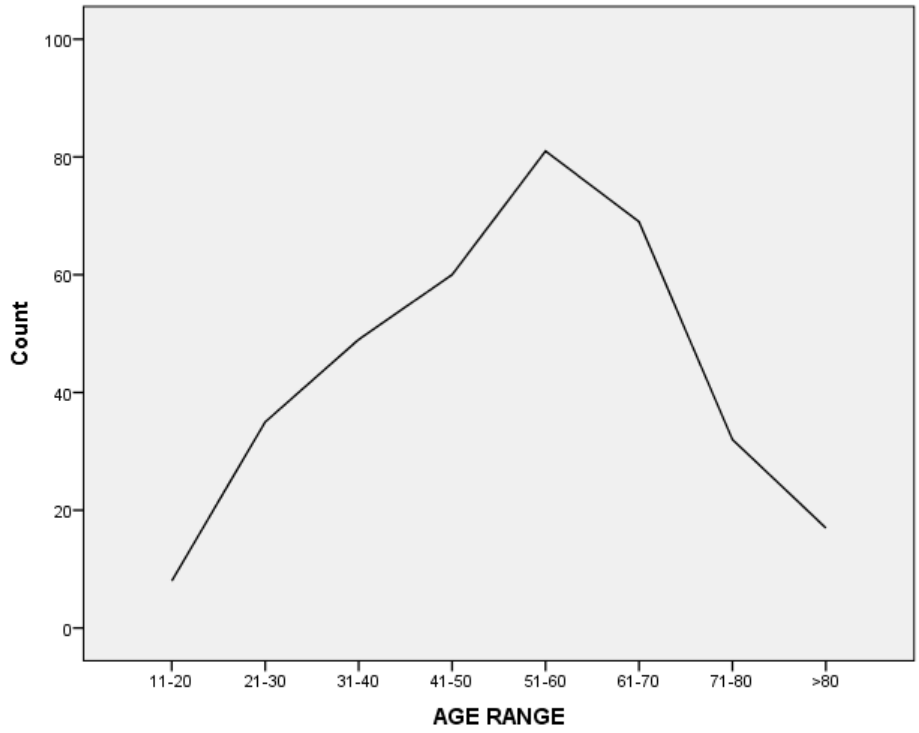

Figure 1: Age trend curve of dyspepsia

Table 2 shows that epigastric discomfort constituted the commonest (96.9%) symptom followed by heart burn (63.1%). Nausea was the least seen symptom of dyspepsia, being absent in 67.3% of the patients.

Table 2: Showing symptoms of dyspepsia present in study participants using the short form Leeds dyspepsia questionnaire

Symptoms	Present (%)	Absent (%)	Total
Heartburn	222 (63.1)	130 (36.9)	352
Epigastric discomfort	341 (96.9)	11 (3.1)	352
Regurgitation	172 (48.9)	180 (51.1)	352
Nausea	115 (32.7)	237 (67.3)	352
Belching	195 (55.4)	157 (44.6)	352

According to figure 2, the top five commonly observed risk factors associated with dyspepsiawere smoking (300/352), unemployment (292/352), obesity (262/352), alcohol intake

(259/352) and Helicobacter pylori infection (292/352); while high pepper intake was the least (126/352). H. pylori infection was positive in 53.1% of the patients.

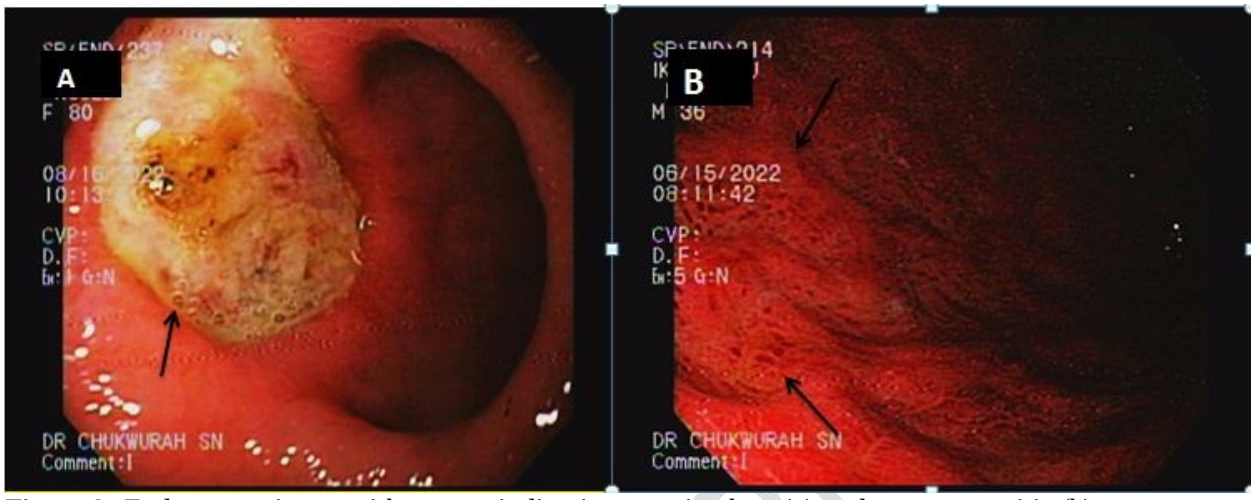

Figure 2: Endoscopy picture with arrows indicating gastric ulcer (a) and severe gastritis (b)

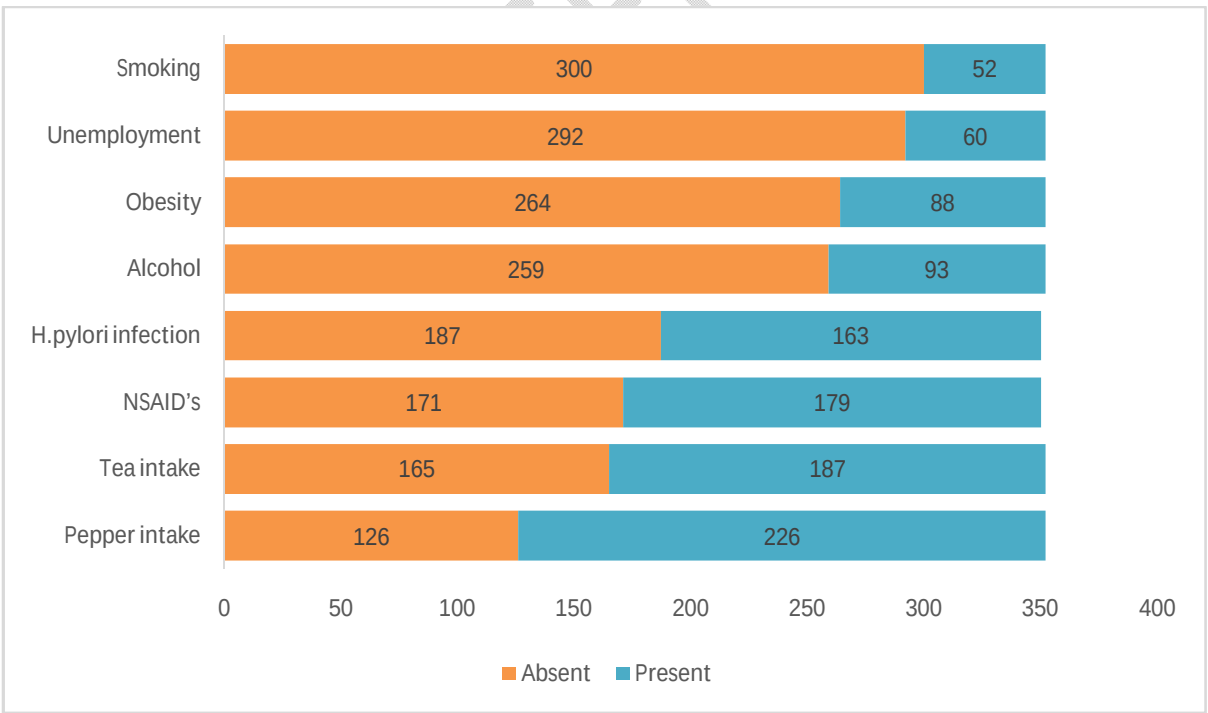

Figure 3 showing the risk factors for dyspepsia

The endoscopic features (Figures 2a-b) were commonly those of chronic gastritis (63.06%). Gastric ulcer was seen in 5.40% while 4.83% had normal endoscopic (Table 3).

Table 3: Distribution of Endoscopy Diagnosis among the Study Participants

Variable	Frequency	Percentage (%)
Chronic gastritis	222	63.06
Duodenal ulcer	9	2.56
Oesophageal cancer	4	1.11
Oesophageal candidiasis	2	0.57
Oesophagealvarices	15	4.26
Gastric cancer	28	7.95
Gastric polyp	5	1.42
Gastric ulcer	19	5.40
Gastroesophageal reflux disease	30	8.52
Normal	17	4.83
Oesophageal ulcer	1	0.28
Total	**352**	**100**

Histologic assessment of the endoscopic biopsies showed varied pathologies; including gastritis and gastric carcinomas (see figures 4a-d).

Chronic gastritis was observed in 51.99%, while Gastric and duodenal ulcers were seen in 5.40% and 2.56% respectively; 27.27% of the biopsies showed normal histologic features. Oesophageal, gastric and duodenal cancers were seen in 1.14%, 6.53% and 0.57% respectively. (Table 4)

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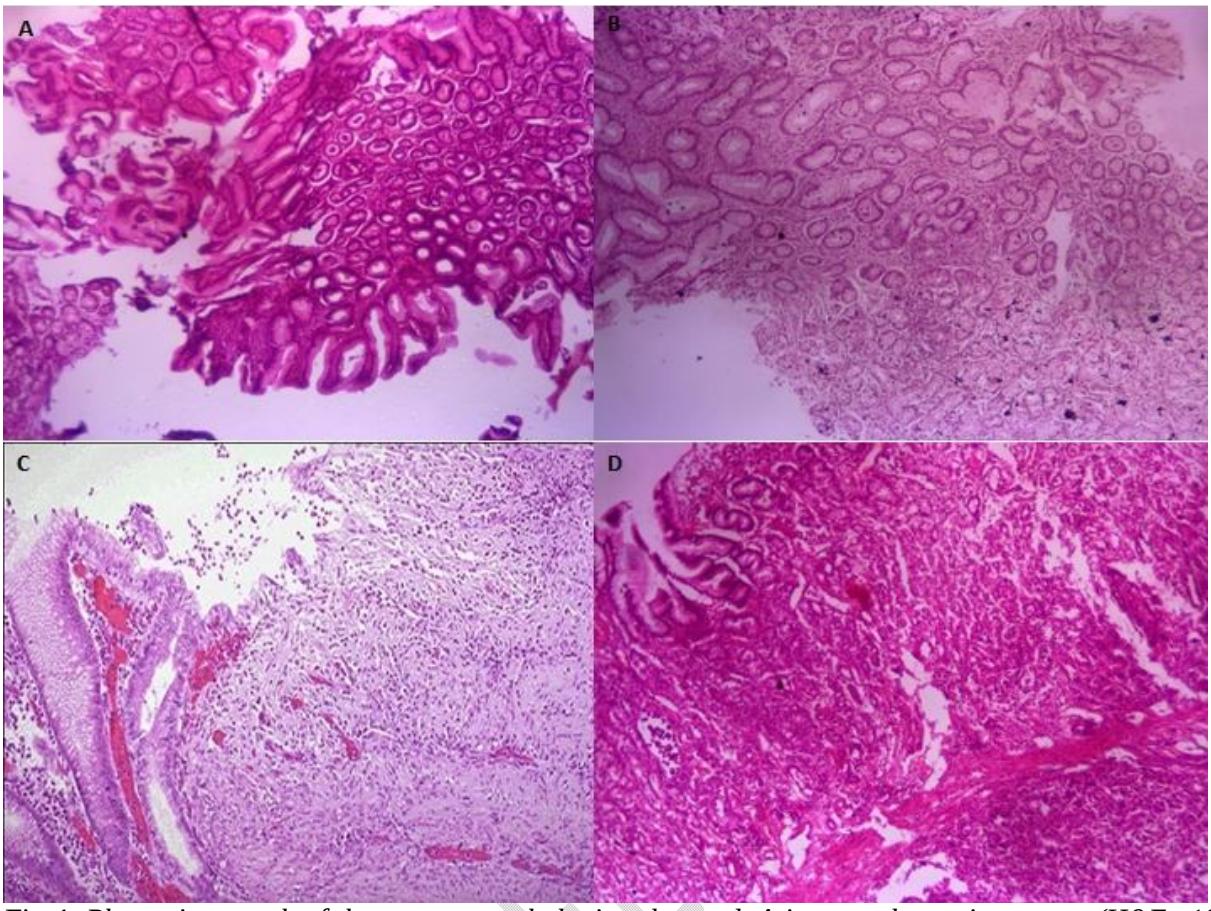

Fig 4: Photomicrograph of the common pathologies observed. A is normal gastric mucosa (H&E x100). B shows gastritis- mild lymphocytic inflammation of the lamina propria, moderate fibrosis and moderate glandular atrophy, but no intestinal metaplasia or dysplasia (H&E x100). C shows gastric ulcer- full thickness epithelial loss with granulation tissue (H&E x100). D shows gastric cancer characterized by dysplastic glands permeating the desmoplastic stroma and the muscularis propria. (H&E x50)

Table 4: Distribution of Histological Diagnosis among the Study Participants

Variable	Frequency	Percent
Chronic esophagitis	2	0.57
Chronic gastritis	183	51.99
Duodenal cancer	2	0.57
Duodenal ulcer	9	2.56
Oesophageal cancer	4	1.14

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Oesophageal candidiasis	2	0.57
Oesophagealvarices	6	1.70
Gastric cancer	23	6.53
Gastric polyp	6	1.70
Gastric ulcer	19	5.40
Normal	96	27.27
Total	**352**	**100**

The histologically diagnosed cases of gastritis were commonly the severe forms (see figure 5).

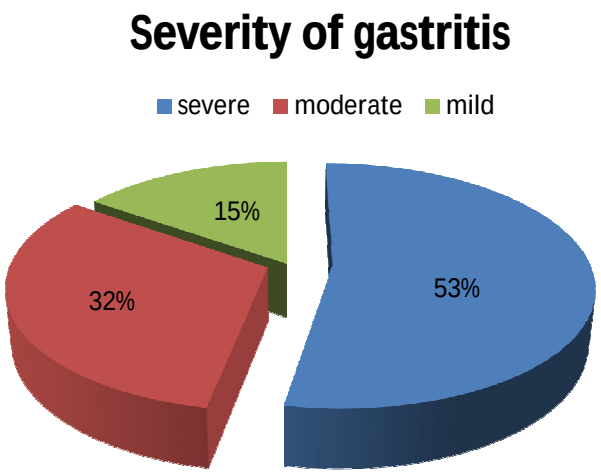

Figure 5: Severity of the histologically diagnosed cases of gastritis

Table 5 shows the correlation between the endoscopic and histopathologic diagnoses. Some (26.58%) of the cases endoscopically classified as chronic gastritis were histologically normal. The Kappa score for correlation was 0.0012 and p-value =0. 442.

Table 5: Table of concord between endoscopy diagnosis and histology diagnosis among the study participants

Endoscopy Diagnosis	Histological diagnosis										
	Duodenal cancer	Duodenal ulcer	Normal	Chronic esophagitis	Chronic gastritis	Esophageal cancer	Esophageal candidiasis	Esophagealvarices	Gastric cancer	Gastric polyp	Gastric ulcer
Chronic gastritis	2	0	59	2	151	0	0	0	1	3	4
Duodenal ulcer	0	**9**	0	0	0	0	0	0	0	0	0
Esophageal cancer	0	0	1	0	0	4	0	0	0	0	0
Esophageal candidiasis	0	0	0	0	0	0	2	0	0	0	0
Esophagealvarices	0	0	7	0	2	0	0	6	0	0	0
Gastric cancer	0	0	0	0	5	0	0	0	21	2	0
Gastric polyp	0	0	0	0	4	0	0	0	0	1	0
Gastric ulcer	0	0	0	0	4	0	0	0	1	0	14
GERD	0	0	12	0	17	0	0	0	0	0	1
Normal	0	0	17	0	0	0	0	0	0	0	0
Total	**2**	**9**	**96**	**2**	**183**	**4**	**2**	**6**	**23**	**6**	**19**

Agreement	**Exp. agreement**	**Kappa score**	**Std. Error**	**z-value**	**p-value**
3.98%	3.68%	0.0012	0.0084	0.15	0.442

GERD= Gastroesophageal reflux disease; Exp=Expected; Std= Standard

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DISCUSSION

Since the introduction of gastrointestinal endoscopy into clinical use in the early 1960s, GI endoscopy has transformed the discipline of gastroenterology and has become a crucial tool in both cancer prevention and the management of GI disorders.[16] Dyspepsia constitutes the major reason for endoscopy in most places. It constituted the commonest (51.9%) indication for oesophagoduodenoscopy (OGD) in Ido Ekiti.[17]

Dyspeptic symptoms can be seen across all age groups. The patients in this study ranged between 15years to 91 years while Oguntoye*et al.*, had a range of 9 years to 89 years.[17] Most patients were in the late 6th decade and early 7th decade. We also observed an increasing trend with increasing patients' age. This is most likely expected as increasing age has been associated with most chronic medical conditions. The general clinical observation of gastrointestinal symptoms increasing with age has also been confirmed by population-based studies.[18,19]In addition, this study was done in Nnewi which is a semi urban town and which also has patients from the surrounding rural villages attending the clinics. Most persons residing in rural areas are the elderly thereby also reflecting in the numbers attending clinics. The findings in this study are similar to the work done by Onyekwere*et al.*, with the majority of the patients being in the middle to elderly age and with a peak in the 5th decade.[20]

The mean age of the study participants was 52.27±16.59 years. This is in keeping with the findings by Oguntoye*et al.*, who had a mean age (±SD) of 52.4(±1.69)[17] and Odeghe*et al.* who had 47.8 (±14.4) among 159 gastroscopies for dyspepsia.[21] It is also in keeping with a hospital-based study done in South-East Asia among patients presenting with dyspepsia where a similar mean age of 56.2 ± 14 and 43.3 ± 14.9 years respectively were found among English and Malay speaking patients.[22]

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There is slight male predominance in this study with a male to female ratio of 1.1:1. The studies done in Ido-Ekiti South-west Nigeria by Oguntoye*et al.,*[17]and in China, southeast Asia,[22]each reportedmale preponderance with male to female ratios of 2.5:1 and 1:1.1 respectively.Male predominance can be attributed to the fact that most of the risk factors such as alcohol, cigarette smoking and use of NSAIDS are generally commoner among this gender.[23] Use of NSAIDs increases with age, primarily for symptoms associated with osteoarthritis and other chronic musculoskeletal conditions.[24] Also the culture of the people where men are in control of finances could be the reason why they present often to the hospital unlike their female counterparts who will have to seek permission from their husbands before presenting to the hospital. However, some other studies have found preponderance of dyspepsia among women.[10, 25-27]A study done by Okonkwo *et al.* in Calabar, in the southern part of Nigeria, among dyspeptics taking non-steroidal anti-inflammatory drugs (NSAIDS), reported slight female preponderance with a male: female ratio of 1:1.3.[12]The difference between this local study and ours may be due to the fact that the Calabar study was limited to patients using NSAIDS. There has not been a convincing mechanism for the gender differences. However, most of the studies that suggested female preponderance were population-based studies and the effect of culture may not be completely ruled out for the reverse findings in hospital-based studies.

The top five most common risk factors for dyspepsia in this study were smoking, unemployment, obesity, alcohol intake and *H. pylori* infection (Figure 2). A population based cross-sectional study done among the Scandinavians showed that NSAID abuse, unemployment and heavy smoking sere of more importance than H. pylori infection.[28]In contrast to our study which observed a combined serology and histology *H. pylori* positivity of 51%, a study done in Northern Nigeria reported serological and histological H. pylori positivity of 93.6% and 80.0%

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respectively among patients with dyspepsia.[29]Higher rate of H. pylori negativity in this study may be attributed to high rate of antibiotic abuse in our environment. Although NSAID abuse was significant here, it was of less significance in contrast to the Scandinavian report.[28]High pepper intakes has also been correlated with dyspepsia inn literatures, and reported as a significant risk factor by Solomon et al.,[30]it is a less significant factor in our study. This shows a geographic variation in incidence which may be culture-related.

The commonest and most distressing presenting symptom was epigastric discomfort. The American College of Gastroenterology and the Canadian Association of Gastroenterology published a joint guideline for the management of dyspepsia and the operational definition for dyspepsia used in the guideline is predominant epigastric pain.[31]A study showed that the three most useful features to predict the presence of major pathology were epigastric tenderness (the single most useful feature), weight loss and burning epigastric pain.[32]These features were selected by stepwise discriminant analysis, which also led to the conclusion that the presence of at least two of these three features is an even more powerful predictor of major pathology.[32]Nausea and regurgitation were not common modes of presentation of dyspepsia in this study. This could be as a result of the presence of other more severe symptoms causing distress thereby masking these other symptoms.

Normal endoscopy findings were observed in 4.83% of the patients. Although, Oguntoye*et al*., reported gastritis as the commonest endoscopic pathology, it constituted 40.4% of patients who had OGD done on account of dyspepsia.[17] The pattern of findings also differed from ours as Duodenal ulcers constituted 8.5% and Gastric erosions constituted 6.4% in the same study [17] The findings of our study also differed from the study done in Ghana which showed normal endoscopy in over 40% of dyspeptic patients and the commonest abnormality being duodenal

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ulcer in 19.6%; gastritis was seen in only 12.7%.[33]The varying patterns of endoscopy may be due to environmental and genetic factors.

Histologic assessment showed no pathology in 27.27% of the patients. Among those with pathology, chronic gastritis was the commonest finding accounting for 51.99% of all patients and 71.9% of those with pathology; Gastric cancer and ulcer were seen in 6.53% and 5.40% of the patients respectively. This agrees with studies done in Bangladesh[34]and South-West Nigeria[35] which histologically assessed biopsy specimens from dyspeptic patients, and both reported chronic gastritis as the commonest pathology. This study also showed that severe form of gastritis (53.01%) was more common. Studies are lacking for adequate comparison of severity of gastritis. However, it is our view that late presentation due to ignorance, poverty and the high unemployment rate may have contributed to high rate of severe gastritis.

Endoscopic diagnosis correlated poorly with the histologic diagnosis in these patients, with kappa score of 0.0012. There were more cases of chronic gastritis seen during endoscopy (222/352) with less reported on histology (183/352). This is in keeping with the study carried out in south west Nigeria in Ekiti State where 162 patients were endoscopically diagnosed as gastritis and 153 were histologically confirmed (concordance rate of 94.4%)[35] and contrary to another study carried out in another state in south west Nigeria which demonstrated that the presence of endoscopic gastritis had a good association with histological gastritis but normal endoscopic appearance was a poor predictor of the absence of histological gastritis.[36]The study by Dawood et al., reported that 65.7% of endoscopically normal gastric and duodenal tissues showed histological lesions, most of which sere chronic gastritis.[37] It is therefore evident that there is poor correlation between the endoscopic diagnosis of dyspepsia and histologic diagnosis

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CONCLUSION:

Most dyspepsiaare due to gastritis, presenting commonly with epigastric pain having smoking and unemploymentas the predominant identified risk factors. However, the concept of dyspepsia requires a proper definition for communication. There is a poor correlation between endoscopic and histologic diagnoses; hence, pathologic assessment remains the gold standard for diagnosis.

Ethical consideration: This was obtained from Nnamdi Azikiwe University Teaching Hospital Ethical committee (NAUTHEC) on 21st June, 2021 with ref no: NAUTH/CS/66/VOL.14/VER 3/173/2021/046. Informed written consents were obtained from the study participants

Data availability: The data used to support the findings of this study are available from the corresponding author upon reasonable request.

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